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BENEFITS OF EXERCISE IN SOLID ORGAN TRANSPLANT RECIPIENTS

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TRAÏNSPLANT: Exercise for Transplantation Patients.

ABSTRACT

Solid organ transplantation is the best treatment option for patients with end-stage disease, but this situation does not come without complications. Weight gain, muscle weakness, reduced exercise tolerance and decreased aerobic capacity are present among recipients of solid organ transplantation. All this is due to prolonged bed rest, inactivity, use of immunosuppressive medication and loss of physical condition and muscle mass. Cardiovascular disease is a major cause of mortality and morbidity in solid organ transplant recipients, with an overall mortality rate of at least 5- to 10-fold greater than the general population. Exercise programs in solid organ transplant recipients report positive effects on the physical condition and quality of life of these patients. Although no significant damage or adverse effects have been reported in the exercise programs included here, it is always necessary to exercise caution and monitoring, and carry them out from a multidisciplinary perspective to avoid possible harm to patients.

Keywords: transplantation, physical activity, quality of life, exercise training

BENEFICIOS DEL EJERCICIO FÍSICO EN PACIENTES TRASPLANTADOS DE ÓRGANO SÓLIDO

RESUMEN

El trasplante de órgano sólido es la mejor opción de tratamiento para los pacientes con enfermedad terminal, pero esta situación no está exenta de complicaciones. El aumento de peso, la debilidad muscular, la escasa tolerancia al ejercicio y la disminución de la capacidad aeróbica están presentes en los receptores del trasplante de órgano sólido. Todo esto se debe al reposo prolongado en cama, la inactividad, el uso de medicamentos inmunosupresores y la pérdida de condición física y masa muscular. La enfermedad cardiovascular es la principal causa de mortalidad y morbilidad en pacientes receptores de trasplantes de órganos sólidos, con una tasa de mortalidad de 5 a 10 veces mayor que la de la población general. Los programas de ejercicio físico en receptores de trasplantes de órganos sólidos, referencian efectos positivos sobre la condición física y la calidad de vida de estos pacientes. Aunque no se han demostrado daños significativos ni efectos adversos en los programas de ejercicios incluidos en esta revisión, siempre es necesario actuar con precaución y monitorizando las variables, llevándolos a cabo desde una perspectiva multidisciplinar, para evitar posibles daños a los pacientes.

Palabras clave: trasplante, actividad física, calidad de vida, entrenamiento físico

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INTRODUCTION

Solid organ transplantation is the treatment of choice for the majority of patients with end-stage organ failure an intervention that can transform their lives and is now the criterion standard of care, but it does not come without complications. According to the National Transplant Organization (ONT), a total of 5,261 solid organ transplants were performed in Spain in 2017: 3,269 kidney transplants, 1,247 liver transplants, 304 heart transplants, 363 lung transplants, 70 pancreas transplants and 8 intestinal transplants. Weight gain, muscle weakness, reduced exercise tolerance, and decreased aerobic capacity are prevalent among solid organ transplant recipients because of prolonged bed rest, inactivity, immunosuppression use, and resultant muscle deconditioning (El-Agroudy, Wafa, Gheith, Shehab El-Dein, & Ghoneim, 2004; Epstein et al., 2004; Julian et al., 1991) .

Metabolic syndrome, a complication of insulin resistance and a sedentary lifestyle, are also common after solid organ transplantation (Kokkinos et al., 2008; Landgraf et al., 1989; Myers et al., 2002). Metabolic syndrome is a common condition among solid organ transplant recipients and it is associated with graft loss and cardiovascular disease (Pedrollo et al., 2016; Tinti, Mitterhofer, & Muiesan, 2012). The components of metabolic syndrome including obesity, hypertension, dyslipidemia, and hyperglycemia, are often exacerbated by transplant-specific factors, such as a sedentary life style and immunosuppression (Anastácio et al., 2014). These metabolic syndrome components are significant independent predictors of posttransplant metabolic syndrome, and the presence of a higher number of metabolic syndrome components is associated with a worse graft function, which may negatively affect the mean survival of transplant recipients (García-Pajares et al., 2016; Lv et al., 2015; Nedbálková et al., 2014; Ruangkanchanasetr et al., 2015).

Morbidity and mortality after solid organ transplant continue to fall, and 1-year patient and graft survival from cadaveric transplants has increased over the past 10 years. Therefore, the long-term focus lies on identifying modifiable risk factors that can be addressed to improve health-related quality of life (HRQoL), morbidity and survival rate (Pilmore, Dent, Chang, McDonald, & Chadban, 2010).

Cardiovascular disease is also a major cause of mortality and morbidity in other solid organ transplant recipients. The 5-year mortality rate from cardiovascular disease in cardiac and kidney transplant recipients are 30% and 15%, respectively (Barker & Jenkins, 2011; States & Transplantation, 2014), with an overall mortality rate of at least 5- to 10-fold greater than in the general population. With improvements in graft survival and a reduction in infection deaths over the past two to three decades, death with a functioning graft, due to cardiovascular disease, is now a critical issue for solid organ transplant recipients (Didsbury et al., 2013). Exercise has a range of health benefits to the general population including improved HRQoL and reduced cardiovascular risk and chronic inflammation (Neale, Smith, & Bishop, 2017).

Despite the magnitude and the severity of cardiovascular diseases in the transplant population, there is a paucity of high-quality evidence regarding interventions for prevention and treatment. Solid organ transplant recipients have been systematically excluded from most trials of physical therapies (Pengel, Barcena, & Morris, 2009). Exercise training consisting in a structured program of physical activity reduces cardiovascular risk factors in the nontransplantation setting (Sharman & Stowasser, 2009).

However, results of the few observational studies that have assessed the outcomes of exercise training in the transplant population are contradictory, which may be due to confusion from the effects of immunosuppression and other comorbidities or residual selection bias (Braith & Edwards, 2000; Marconi & Marzorati, 2003; Wickerson, Mathur, & Brooks, 2010). Many solid organ transplant patients wish to either return to, or begin, new sporting activities to improve their health after a transplant, and this higher intensity exercise may have more unanticipated effects than activity at lower levels (Neale et al., 2017).

The aim of this review was to determine the health benefits of exercise programs in solid organ transplant recipients.

Exercise capacity

There was substantial variation in the length of time between the surgery and the beginning of the exercise program. In a recent review, Didsbury et al. (2013) found that exercise training that commenced within 1 year after cardiac transplantation was associated with significant improvements in the overall VO2max with exercise compared with standard care, whereas those patients who commenced the exercise program 12 months after surgery showed no significant improvement in their functional capacity.

Interventions comprising aerobic or combined aerobic and resistance exercise have consistently been shown to improve workload and muscle strength. Durations of between 12 weeks and 12 months and both home-based and supervised training have been effective in all types of transplant recipients. These improvements are also translated into a significant improvement in physical performance in a variety of tests such as the 6-Minute Walk Test (6MWT) and the capacity to exercise until exhaustion (Neale et al., 2017).

Regular exercise has positive effects on cardiovascular risk in the general population (Powers, Lennon, Quindry, & Mehta, 2002) and now, the focus has switched to analyzing the effect on transplant recipients. The observed benefits are predominately driven by the amelioration of peripheral insulin sensitivity, insulin-mediated transport of glucose to muscles, increased transport of lipids to the liver, slower heart rates, and improved autonomic system functioning associated with increased fitness (Carnethon et al., 2003).

Kidney transplantation

The Guideline for the Care of Kidney Transplant Recipients recommends to adopt a healthy lifestyle with regular physical activity (KDIGO, 2009). However, patients undergoing kidney transplantation typically have a low physical activity (Hernandez Sanchez et al., 2016), a poor exercise capacity and a sedentary lifestyle (Dontje et al., 2014; Mosconi et al., 2014), all of which have been associated with an increased risk of cardiovascular mortality (Zelle et al., 2011), metabolic complications and sarcopenia (Roi et al., 2014).

Patients with chronic kidney disease and those on dialysis in particular have an elevated cardiovascular risk compared to the general population (Matsushita et al., 2010). Kidney transplantation improves survival (Wolfe et al., 1999) and quality of life (QoL) (Von Der Lippe et al., 2014) and reduces cardiovascular events (Oniscu, Brown, & Forsythe, 2004) compared to individuals on dialysis; although outcomes still remain poorer than in the general population (Bottomley & Harden, 2013), being the rate of cardiac death 10 times higher and the annual rate of fatal or nonfatal cardiovascular events 50 times greater than that of the general population. It is thought that this is due to traditional cardiovascular risk factors, such as hypertension and dyslipidemia, but nontraditional risks such as immunosuppression (Boots, Christiaans, & Van Hooff, 2004), chronic inflammation (Abedini et al., 2009), and altered hemostasis (Opatrny, Zemanova, Opatrna, & Vit, 2002) also play an important role. Weight gain, obesity, diabetes, hypertension and metabolic syndrome are predominant features in these patients and are associated with bad outcomes, including death, cardiac events and graft loss (Kumar et al., 2012). In addition, immunosuppressive therapy may contribute to the development of dysmetabolism and a worsening of sarcopenia (Mosconi et al., 2014), and low muscle mass has been associated with poor survival after kidney transplantation (Oterdoom et al., 2008).

Prospective studies have investigated the effects of prescribed exercise programs on physical fitness, QoL, and cardiovascular risk factors and outcomes (Takahashi, Hu, & Bostom, 2018). In kidney transplantation, there are no overall significant effects of exercise on blood pressure (Patricia L Painter et al., 2003) with both a supervised 6-week aerobic training and a 1-year home-based aerobic program, yielding insignificant results in those patients undergoing the intervention (133/87 at baseline to 132/89 at 12 months) compared to the control group receiving usual care (138/88 to 133/90). Additionally, exercise programs for kidney transplantation patients do not seem to interact with antihypertensive medications either, with the number of antihypertensives being similar at all time-points and between groups (Patricia Lynn Painter et al., 2002). Physical performance outcomes that have been measured have varied greatly, with the most common being VO2max and muscle strength. Exercise interventions have ranged from interval training and active video gaming to a personalized exercise prescription involving collaboration between a transplantation center, a sports medicine center, and a gymnasium (Roi et al., 2014).

Many of the prospective studies have observed that compared to usual care, a prescribed exercise program was effective in improving physical performance (Kouidi, Vergoulas, Anifanti, & Deligiannis, 2013; Riess et al., 2014), subjective QoL, and various fitness parameters (Karelis, Hébert, Rabasa-Lhoret, & Räkel, 2016). One-year of home aerobic training also resulted in an improvement in peak torque (per body weight) in the intervention group (46.7 to 57.6 Nm) compared to the control group (45.6 to 50.4 Nm; $p < 0.003$) (Painter et al., 2002).

Furthermore, a 24-week study of treadmill exercise alone revealed that exercise time to exhaustion improved (12 min; $p < 0.001$), and there were also large increases seen in isokinetic muscle function in both the quadriceps and hamstrings ($p < 0.001$ to $p < 0.0001$), although values were still lower than in the untrained non- transplanted healthy control group. Muscle biopsies showed an unexpected rise in type 2 muscle fibres and low oxidative capacity, suggesting that enhanced muscle contractile function is partly responsible for improved overall performance (Kempeneers et al., 1990).

In kidney transplant, a thrice-weekly strengthening focused exercise program of 6 months duration found that upper-extremity muscle strength increased more in the rehabilitation group compared to the control group, although this increase did not reach significance (Korabiewska, Lewandowska, Juskowa, & Białoszewski, 2007). Similarly, a 7-week isokinetic bicycle-based exercise program investigating outcomes in those patients on prednisolone compared to those on steroid-sparing regimes found improvements in peak torque (at 60°) in both groups (prednisolone-free: 236–289 Nm after training completion; $p < 0.005$; prednisolone: 207–237 Nm; $p < 0.005$) and in total work output (at 180°/s) (prednisolone-free: 3563–4584 J after training completion; $p < 0.001$; prednisolone: 2712–3587 J; $p < 0.001$) (Horber et al., 1987). Benefits were also seen in a study of the Don Jeon program (You, Chung, So, & Choi, 2008) for a duration of 9 weeks with a once-a-week supervised session and daily activity at home, in which grip strength ($p < 0.001$), back muscle strength ($p = 0.01$), and sit-and-reach distance ($p < 0.001$) all improved in the intervention group compared to those receiving usual care.

Heart transplantation

Reduction in exercise capacity is common after solid organ transplantation, particularly after heart transplantation. This reduction in exercise tolerance is in part due to the effects of immunosuppressive medication, deconditioning due to prolonged hospital stay, graft dysfunction, and cardiac denervation (Wilson et al., 1991). In heart transplant patients, exercise capacity is affected by denervation, which in turn reduces the overall responses to exercise compared with the general population. Additionally, the anatomy is not completely restored and during the operation, the heart is surgically denervated, and this is not entirely corrected. In the postoperative months, some patients show signs of partial cardiac reinnervation, which may serve to, in part, normalize their responses to exercise. Heart transplant recipients also often experience diastolic dysfunction. The underlying causes are likely to be multifactorial including hypertension, episodes of rejection, and vasculopathy of the allograft. These factors affect the function of the transplant directly and are likely to influence the response to exercise (Neale et al., 2017).

Reduction in exercise capacity is a particular concern for heart and lung transplant recipients who exhibit exercise capacity in the range of 40% to 60% of normal postoperatively (Mathur, Reid, Levy, 2004; Reinsma et al., 2006), which may impact on the overall well-being and HRQoL. Therefore, strategies to improve exercise capacity are considered as research and clinical priorities in thoracic organ recipients. Emerging data suggest that exercise training after transplantation improves exercise capacity, as assessed by the 6MWT, the quadriceps force, the total walking time, and the self-assessed level of physical function, measured up to 1 year after transplantation (Langer et al., 2012). Aerobic exercise after heart transplantation has a positive effect to increase physical capacity and prevent long-term complications such as hypertension and diabetes, but heart transplantation recipients' physical capacity still remains below normal in most studies (Hsieh, Wu, & Chao, 2011).

High-intensity interval training is proven to be a more efficient exercise modality than moderate-intensity continuous training in order to increase VO2peak, shown in patients with heart failure, cardiovascular disease and metabolic disease, as well as in healthy individuals. This new knowledge has had a great impact on how general cardiac rehabilitation programs are organized today (Yardley, Gullestad, & Nytrøen, 2018).

The introduction of a supervised exercise training program after heart transplantation, especially early after transplantation, has consistently shown to improve the VO2max up to 12 months after transplantation (Haykowsky, Taylor, Kim, & Tymchak, 2009; Hermann et al., 2011). These studies in the heart transplant population demonstrated, on average, a 10.2% increase in VO2max among those who received structured exercise training and rehabilitation after the surgery compared with recipients who did not. A 6-month structured aerobic and strength training program designed for heart transplantation recipients revealed that peak workload increased in the exercisers (59 to 94 W) compared to the usual care group (66 to 78 W; $p = 0.01$) and the duration of exercise performed also improved (exercisers: 6.9 to 9.0 min; controls: 7.2 to 8.3 min; $p = 0.07$) (Kobashigawa et al., 1999).

In heart transplantation patients, a 6-month study of cycle-based moderate intensity exercise 5 times a week at home found that in the training group, physical performance improved significantly, with exercise time (7.65–11.40 min; $p < 0.01$) and maximal workload (75 W–105 W; $p < 0.01$) both showing improvements, and the anaerobic threshold was reached at higher workloads (50–75 W). Physical performance did not improve in the control group, with VO2peak (14.33–15.60 mL/kg per min), exercise time (8.00–8.50 min) and peak workload (70–78 W) remaining comparable to baseline (Bernardi et al., 2007).

Another study of 10 weeks of aerobic exercise 2 to 3 times per week found a significant increase in peak heart rate in the exercising group (128–146 beats per min) compared to the control group (136–142 beats per min; $p < 0.05$) and in the duration of the exercise to exhaustion test (exercisers: 9.2–10.7 min; control: 8.5–8.8 min; $p < 0.05$) (Keteyian et al., 1991). Further case reports have shown that after an intensive endurance training program, heart transplant recipients are able to improve maximal power, oxygen consumption, resting and submaximal heart rate, and ventilator anaerobic threshold.

Lung transplantation

Evidence summaries, however, showed a lot of variability regarding the effects different training programs have on the selected training outcomes for lung transplantation patients. This seems to indicate that not all exercise programs for lung transplantation patients are equally effective (Wallen et al., 2016). These differences in effect might be due to the confusion between exercise and physical activity. Physical activity is "*any bodily movement produced by skeletal muscle resulting in energy expenditure*" whereas exercise is defined as *"a planned, structured, and repetitive subset of physical activity with an identifiable aim to improve or maintain physical fitness*" (Knols, Fischer, Kohlbrenner, Manettas, & de Bruin, 2018, p.2).

For clinicians, selection and replication of successful exercise programs is important. In addition to evaluating and judging the results of systematic reviews, clinicians should, therefore, be able to identify replicable interventions for the translation of useful interventions in clinical settings (Hoffmann et al., 2014).

For patients with chronic lung conditions, transplantation offers the chance of improving QoL, morbidity, and mortality. In 2017, according to the National Transplant Organization, there were 668 people currently waiting for a transplant in Spain, with the most common underlying diagnoses being congenital disease, chronic obstructive pulmonary disease, diffuse interstitial lung disease and cystic fibrosis. Survival and HRQoL in patients with end stage pulmonary disease is expected to improve following lung transplantation (Hatt, Kinback, Shah, Cruz, & Altschuler, 2017). Both showing improvements in early (less than 1 year) and in late (more than 1 year) lung transplantation patients, it seems feasible, safe, and effective to perform physical exercise following transplantation (Wallen et al., 2016). When lung transplantation patients exercisers and non-exercisers are compared, there is some evidence available supporting the idea that structured physical exercise programs improve maximal exercise capacity, physical function, muscle strength, and bone mineral density (Langer et al., 2012) and, thus, favors exercise regarding amelioration of physical and functional task capacities. Such improvements seem especially apparent in patients perceiving their physical functioning as low (Knols et al., 2018).

Lung transplantation is a highly complex procedure that carries considerable perioperative and postoperative risks. It is a treatment option for patients whose pulmonary function, exercise capacity, and QoL are drastically restricted, and their predicted 5-year survival rate is less than 50% (Hartert et al., 2014).

There are 3 types of lung transplant: single lung transplantation, double lung transplantation, and simultaneous heart and lung transplantation, with the selection depending on the underlying pathology. The 1- and 5-year survival rates for single lung transplantation and double lung transplantation are 77% and 59%, respectively (Harringer & Haverich, 2002). Infection (38%), rejection (29%), malignancy (15%), and cardiovascular disease (10.9%) are the main contributors to postoperative morbidity and mortality postoperatively (Hartert et al., 2014), as well as organ-specific complications such as obliterative bronchiolitis, all of which may be influenced by physical activity. Posttransplant rehabilitation has recently been the focus to optimize long-term outcomes and promote physical and psychological measures, as these still remain impaired despite transplantation, with most lung transplant recipients remaining sedentary 3 to 6 months after transplant (Langer et al., 2009; Wickerson et al., 2010).

Both, researchers wanting to replicate successful intervention research and clinicians wanting to apply these interventions in their practice, need detailed descriptions of the applied procedures in the intervention program. However, many published intervention researches fail to conform to requirements that would guarantee full replicability (Hoffmann et al., 2014).

When reporting the results of a physical exercise program, it is important to document the core principles of the training used and how these were considered for the population under investigation. These principles of physical exercise are specificity, overload, progression, initial values, reversibility, and diminishing returns. When designing a physical exercise intervention, adhering to the principles of physical exercise ensures that an appropriate dose and type of exercise can be applied to accomplish a predetermined training goal; e.g., setting goals may relate to endurance, strength and/or physical function. Furthermore, it is of relevance to report the frequency, intensity, time and type (FITT) of the physical exercise intervention. Only if physical exercise training programs are documented in sufficient detail, their replication can be warranted, and clinicians and researchers are enabled to apply these effective interventions (Hoffman, 2014; Hoffmann et al., 2014). For the exercise interventions to be replicable there should at least be reporting of the FITT components (Baschung Pfister, de Bruin, Tobler-Ammann, Maurer, & Knols, 2015). This holds true for both more traditional forms of exercise and for innovative training approaches in which for example novel technology is used; e.g., exergame based training (Knols, Vanderhenst, Verra, & de Bruin, 2016).

Randomized controlled trials theoretically provide the best evidence regarding the effectiveness of physical exercise interventions; however, inadequate methodological approaches may overstate treatment effects and bias results (Baschung Pfister et al., 2015). An intervention of mixed aerobic and strengthening training initiated in the first few weeks after a transplant also reported an improvement in performance in the 6MWT (451 m at 1 month to 543 m at 3 months after transplantation). Improvements between all time points were statistically significant (p < 0.0001), although with no control group for comparison, it is difficult to make assumptions from this study that lung transplant patients would not have shown improvement after transplantation without the intervention (Munro, Holland, Bailey, Button, & Snell, 2009).

A 12-week study of a thrice-weekly cycling program found that endurance time improved in lung transplant patients to the same extent as healthy subjects but with greater variability between patients (lung transplant patients: +9 min; healthy control: +8 min; p < 0.05). Additionally, muscle strength improved significantly in lung transplant patients, with similar increases also seen in the healthy controls (lung transplant patients: +4.6 kg; p = 0.001; controls: +3.1 kg; p = 0.047), leading to a recovery of muscle strength compared with the healthy subjects' initial value. In lung transplant patients, the percentage of type I fibre (+7%, p = 0.10) and the type II fibre diameter (−3 μm,

p = 0.10) also increased, although the changes did not reach statistical significance (Vivodtzev et al., 2011). Three months of supervised combined aerobic and resistance training resulted in an improvement in performance in the 6MWT at 1 year in the lung transplant patients undergoing exercise training (56% predicted [pred] – 86% pred) compared to the controls receiving usual care (51% pred – 74% pred; p = 0.002), as well as peak workload (exercisers: 47% pred – 69% pred; controls: 39% pred – 53% pred; p = 0.043) and quadriceps force (exercisers: 63% pred – 92% pred; controls: 56% pred – 71% pred; p = 0.001) (Langer et al., 2012).

Liver transplantation

A recent observational study reported a significant increase in the incidence of metabolic syndrome after liver transplantation, from 5.1% before transplantation to 50% after transplantation, with an associated increase in cardiovascular morbidity by at least 3-fold compared with those without metabolic syndrome (Laish et al., 2011). Liver transplantation offers patients with end-stage liver disease improved morbidity and mortality and is now an established procedure in the developed world. Obesity and the development of metabolic syndrome are well recognized after liver transplantation, with an increasing body mass index seen in the first few years after surgery and 22% of the previously normal-weight individuals becoming obese within 2 years (Everhart et al., 1998).

Independent predictors of obesity include episodes of acute rejection and a higher dose of prednisolone. In liver transplantation recipients, increased body mass index at 1 year accurately predicts the development of metabolic syndrome, and one-third will have cardiovascular disease at 8 years. Therefore, addressing weight gain in the early postoperative period should be seen as a priority to reduce cardiovascular disease in the future. Liver transplantation has also been shown to improve markers of QoL, including self- reported physical health, daily activities, general HRQoL, and social functioning (Bravata, Olkin, Barnato, Keeffe, & Owens, 1999; Fussner et al., 2015).

Various authors have applied a 6-month exercise program, all of whom have achieved substantial improvements in parameters such as VO2max, strength and HRQoL. This latter measurement was assessed with self-perceived health questionnaires like the SF-36 (Beyer et al., 1999; van den Berg-Emons et al., 2014).

After 24 sessions of aerobic treadmill-based exercise, the exercising group increased their walking distance (baseline: 453.6 m; after the program: 582.5 m; $p < 0.05$) compared to the controls receiving usual care (baseline 516.5 m; after the program: 517.7 m) (Garcia, Veneroso, Soares, Lima, & Correia, 2014). In liver transplantation patients, 10 months of home-based aerobic exercise led to a significant increase in quadriceps strength in the exercising group over time (36.4 Nm to 44.1 Nm; $p < 0.001$), although this was not significantly different from the control group (39.5 Nm to 44.6 Nm) (Krasnoff et al., 2006).

A supervised 12-week combined aerobic and strength training program with lifestyle counseling with no control group did find a nonsignificant trend towards improvement in quadriceps strength (baseline: 1.3 Nm/kg; after program: 1.4 Nm/kg; $p = 0.058$), although improvements in workload (baseline: 1.6 W/kg; after program: 1.7 W/kg; $p = 0.004$) and performance in the 6MWT (baseline: 546.5 m; after program: 578 m; $p = 0.004$) were significant (van den Berg-Emons et al., 2014). The study by Tomás, Santa-Clara, Monteiro, Barroso, and Sardinha (2011) applied a training program to a patient who received a transplant due to familial amyloid polyneuropathy, from 6 to 12 months after the intervention. The program consisted of moderate intensity aerobic exercise, that was not specified in the text, with a frequency of 3 one-hour weekly sessions. After 6 months, fatigue had dropped 31%, VO2max had increased by 21.6%, quadriceps strength had improved by 28.3%, and the patient walked 21.3% more distance in the 6MWT.

Van den Berg-Emons et al. (2014) conducted a study of 18 liver transplant recipients, who completed an exercise program with 2 one-hour sessions per week for 12 weeks. The exercise program included aerobic exertion and strength training. The former involved ergometer cycling for 30 min, starting at an intensity of 40%–50% of the heart rate reserve, using the Karvonen method. After 12 weeks, patients had to pedal at 60% of the heart rate reserve. The strength training lasted 30 min per session and focused on the large muscle groups. The intensity and number of repetitions increased over the 12-week period from a series of 10–15 repetitions at 30% of one repetition maximum (1 RM), to 3 series of 20 repetitions at 60% of 1 RM. In order to determine the changes between the start and end of the program, aerobic capacity was measured by means of a maximum exertion test on a cycloergometer and the 6MWT. Maximum strength was measured in the quadriceps and hamstring muscles with an isokinetic dynamometre (Biodex). The test was done 5 times at 60º/s. Body composition and fatigue were also evaluated. The results of this study were satisfactory. The VO2max increased by 10% and strength only increased in the hamstrings by 10%. There were no changes in body mass index, although the percentage of body fat decreased significantly.

A randomized 24-week combined resistance and aerobic-based regime based either at home or supervised in a clinical setting revealed no significant improvement in performance in the 6MWT between the supervised exercisers (baseline: 506.2 m to after program: 573.3 m), home-based exercisers (baseline: 491.2 m to after program: 550.5 m) or the control group receiving usual care (baseline: 530.9 m to after program: 553.6 m; $p > 0.05$) or in the quadriceps strength (supervised: baseline: 506.2 Nm to after program: 573.3 Nm; home: baseline 491.2 Nm to after program: 550.5 Nm; control: baseline: 530.9 Nm to after program: 553.6 Nm; $p > 0.05$) (Tomás et al., 2013).

Conclusions

Exercise training improved cardiorespiratory fitness, muscle strength and functioning QoL of solid organ transplant patients. Incorporation of exercise into the routine postoperative care of transplant recipients should be strongly considered owing to the improvement in many aspects of the well-being in these patients and the absence of significant complications or adverse effects. High intensity interval training is a feasible and efficient modality of exercise among maintenance heart transplantation recipients, but the mechanisms behind this effect are poorly understood.

The lack of information on hard outcomes and long-term safety represents the major limitation and long-term evidences on safety and hard outcomes are needed. Although no significant harm or adverse effects were reported in the studies here included, caution and monitoring are always necessary and an uncontrolled increase in the dose of physical activity at this time should be considered detrimental for the solid organ transplant recipient' patients.

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